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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,807	TJOA ET AL.	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-29* is/are pending in the application.

4a) Of the above claim(s) *4-7,10-12,16 and 24-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 8-9, 13-15, and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 11/9/07 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/9/07 has been entered.

Claims 1, 9, and 19-20 have been amended.
Claims 1 and 3-29 are pending.

Claims 4-7, 10-12, 16, 24-29 stand withdrawn from further consideration pursuant to 37 CFR 1.14209 as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 1, 3, 8-9, 13-15, 17-23 are under examination.

2. The rejections of the claims under 35 U.S.C. 102 and 103 are withdrawn in view of Applicant's amendment to the claims. Specifically, Sallusto et al. do not teach an immature dendritic cell having CD1a on the surface.

3. The following are new grounds of rejection.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 8-9, 13-15, 17-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for differentiating human monocytic dendritic cell precursors into immature dendritic cells having CD1a on the cell surface,

does not reasonably provide enablement for:

a method for differentiating monocytic dendritic cell precursors into immature dendritic cells having CD1a on the

cell surface.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient data to enable claims drawn to the method as broadly claimed. The instant claims are drawn to a method of producing CD1a expressing dendritic cells comprising culturing non-activated dendritic cell precursors in the presence of GM-CSF in the absence of additional cytokines. However, the claims encompass culturing any monocytic dendritic cell precursor from any species, including mouse. CD1a is a marker of human dendritic cells that is not expressed by mouse dendritic cells (see Strominger et al., 2003). Thus, it is unclear how the claimed method could function using precursors other than human precursors. Thus, based on the state of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that human monocytes cultured in the presence of

GM-CSF results in the generation of a CD1a expressing dendritic cell. No examples are provided that culture of other types of precursors can result in a CD1a expressing dendritic cell. Accordingly, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 8-9, 14, 17-19, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Bernard et al., 1998 (of record).

Bernard et al. teach a method comprising culturing non-activated monocytes (i.e. a monocytic dendritic cell precursor) with GM-CSF alone in a TEFLON^{tm} culture bag (i.e. a bag comprising PFTE, see page 18-19 in particular). Bernard et al. further teach that the culture system is adherent free, and that the resulting cells express CD1a (see Fig. 2, in particular). Bernard et al. also teach that the monocytes are isolated by apheresis (see page 18 in particular). Bernard et al. further teach contacting the CD1a+ cells with tetanus toxoid (i.e. a bacterial antigen, see page 22 in particular). Additionally, the instant claims are drawn to a method of differentiating dendritic cells employing a dendritic cell precursor (i.e. a method of using a product made by a particular process). Thus, the method by which the monocytic precursor is produced does not carry patentable weight in the absence of a structurally difference (see MPEP 2113). The monocytic dendritic cell precursors of Bernard et al. are the same as those produced by tangential flow filtration. Additionally, while Bernard et al. do not characterize the CD1a+ cells as immature dendritic cells, they must inherently be immature dendritic cells, since they are produced by a method identical to that of the instant claims.

Thus, the reference clearly anticipates the invention.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3, 8-9, 13-14, and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matera et al., 2000, in view of Bernard et al., 1998(of record).

Matera et al. teach a method of differentiating dendritic cells comprising providing a population of peripheral blood monocytes that have been selected by magnetic sorting (i.e. non-activated), and contacting said monocytes with GM-CSF in the absence of additional cytokines (see page 30 and 31 in particular). Matera et al. also teach culturing in a serum free medium (see page 31 in particular). Matera et al. further teach that the dendritic cells generated by culture with GM-CSF alone express CD1a (see page 31 in particular). Additionally, the instant claims are drawn to a method of differentiating dendritic cells employing a dendritic cell precursor (i.e. a method of using a product made by a particular process). Thus, the method by which the monocytic precursor is produced does not carry patentable weight in the absence of a structurally difference (see MPEP 2113). The monocytic dendritic cell precursors of Matera et al. are the same as those produced by tangential flow filtration.

Matera et al. do not teach a low avidity culture vessel comprising PFTE.

Bernard et al. teach a method to generate dendritic cells from purified blood monocytes by culturing in a TEFLON^{tm} (i.e. comprising PFTE) bag. Furthermore, Bernard teaches that said method meets good laboratory practice (GLP) procedures necessary for the clinical use of dendritic cells (see pg. 23).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the dendritic cells taught by Matera et al., using the TEFLON^{tm} culture vessel, as taught by Bernard. The ordinary artisan at the time the invention was made would have been motivated to do so, since Bernard teaches that this method is useful for clinical purposes, since it involves the large scale differentiation of dendritic cells in a culture system that meets GLP procedures (see abstract and pg. 23). Moreover, one of ordinary skill in the art would have a reasonable expectation of success.

8. Claims 19-23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Matera et al. and Bernard et al., as applied to claims 1, 3, 8-9, 13-14, and 17-18 above, in further in view of Bosch et al., 2001 (of record).

The teachings of Matera et al. and Bernard et al. are described above.

They not teach generating maturing the dendritic cells with IFN-γ and BCG.

Bosch teaches that dendritic cells can be matured with a combination of INF-γ and BCG (i.e. a bacterial antigen). Additionally, Bosch teaches that maturation with IFN-γ and BCG results in a dendritic cell population that can induce an immune response against a tumor antigen in cancer patients (i.e. a therapeutically useful dendritic cell population).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a dendritic cell, as taught by Matera et al. and Bernard et al., followed by maturation with BCG and IFN-γ as taught by Bosch. The ordinary artisan would have been motivated to do so,

since Bosch teaches that IFN-γ and BCG are extremely potent maturation agents that result in a dendritic cell population that can induce an immune response against a tumor antigen in cancer patients (i.e. a therapeutically useful dendritic cell population). Moreover, one of ordinary skill in the art would have a reasonable expectation of success, since Bosch teaches the effectiveness of these techniques in the generation of dendritic cells.

9. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Matera et al. and Bernard, as applied to claims 1, 3, 8-9, 13-14, and 17-18 above, and further in view of Lewalle et al., 2000 (of record).

The teachings of Matera et al. and Bernard et al. are described above.

They do not teach using a cryopreserved cell population to generate dendritic cells.

Lewalle teaches the generation of dendritic cells from frozen peripheral blood mononuclear cells (see pg. 70). Furthermore, Lewalle teaches that many clinical protocols are based on sequential injections of dendritic cells, and therefore it would be of practical importance to have frozen aliquots of the same peripheral blood mononuclear cells for these purposes (see pg. 70).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the dendritic cell taught by Matera et al. and Bernard et al., using frozen peripheral blood mononuclear cells, as taught by Lewalle. The ordinary artisan at the time the invention was made would have been motivated to do so, since Lewalle teaches that many clinical protocols are based on sequential injections of dendritic cells (see pg. 70), and therefore it would be of practical importance to have frozen aliquots of the same peripheral blood mononuclear cells for these purposes. Furthermore, the ordinary artisan would have had a reasonable expectation of success, since Lewalle teaches that dendritic cells derived from frozen peripheral blood mononuclear cells retain their functional capacity (see pg. 73).

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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12/20/07
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